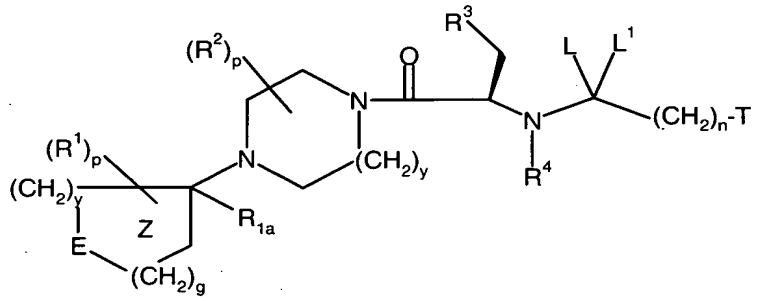
AMENDMENTS TO THE CLAIMS

WHAT WE CLAIMS IS:

1. (Original) A compound of formula I:



(I)

or a pharmaceutically acceptable salt, solvate or stereoisomer thereof,

wherein:

L and L^1 are both hydrogen or combine together to form an oxo group;

E is: O, S, NR^{1b}, SO, SO_2, CR^9, or $C(R^9)_2$, provided that when E is CR^9, or $C(R^9)_2$, R^9 may combine with an adjacent R^1 to form a 5, 6, or 7-member saturated or unsaturated carbocycle;

wherein the Z ring has 0, or 1 double bond;

R^1 is selected from the group consisting of:

hydrogen,

C_1-C_8 alkyl,

C_2-C_8 alkenyl,

C_2-C_4 haloalkyl

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

aryl,

$C(O)OC_1$-C_8 alkyl,

wherein phenyl, aryl, alkenyl, and cycloalkyl groups are optionally substituted with hydroxy, halo, C_1-C_8 alkyl, C_1-C_4 alkoxy, C_2-C_4 haloalkyl, and (D)C_3-C_7 cycloalkyl provided that the halo, hydroxy are not substituted on a carbon atom adjacent to a heteroatom;

R_{1a} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

(D)aryl,

(D)heteroaryl;

(D)C(O)C_1-C_4 alkyl,

(D)C(O)OC_1-C_4 alkyl,

$(CH_2)_mN(R^8)_2$,

$(CH_2)_mNR^8C(O)C_1$-C_4 alkyl,

$(CH_2)_mNR^8SO_2(C_1$-C_4 alkyl),

$(CH_2)_mOR^8$,

$(CH_2)_mSC_1$-C_4 alkyl,

$(CH_2)_mSO(C_1$-C_4 alkyl),

$(CH_2)_mSO_2(C_1$-C_4 alkyl), or

$(CH_2)_mSO_2\ N(R^8)_2$;

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to five substituents independently selected from the group consisting of perfluoroC_1-C_4 alkoxy, halo, hydroxy, C_1-C_8 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl; provided that halo and hydroxy groups are not substituted on a carbon atom adjacent to a heteroatom;

R^{1b} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

SO_2(C_1-C_8 alkyl),

(D)C(O)C_1-C_4 alkyl,

(D)C(O)OC_1-C_4 alkyl,

(D)CON(R^8)2, or

SO_2(D)phenyl, wherein the phenyl group is optionally substituted with one to five substituent selected from halo, and C_1-C_8 alkyl;

R^2 is: hydrogen,

C_1-C_8 alkyl,

CONHC_1-C_4 alkyl,

(D)phenyl, oxo, or

(D)C_3-C_7 cycloalkyl, provided that when R^2 is oxo, R^2 is on one of the ring carbon atoms adjacent to the nitrogen atom bearing the Z ring;

R^3 is: phenyl, aryl or thienyl;

wherein phenyl, aryl and thienyl are optionally substituted with one to three substituents independently selected from the group consisting of:

cyano, perfluoroC_1-C_4 alkoxy, halo, C_1-C_8 alkyl, (D)C_3-C_7 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl;

R^4 is: hydrogen,

C_1-C_8 alkyl,

$CH_2(CH_2)_mC_1$-C_4 alkoxy,

C(O)C_1-C_4 alkyl or

C(O)OC_1-C_4 alkyl;

R is: hydroxy,

halo,

C_1-C_8 alkyl,

C_2-C_8 alkenyl,

C_1-C_8 alkoxy,

C_1-C_4 haloalkyl,

(D)C_3-C_7 cycloalkyl,

(D)aryl,

(D)heteroaryl;

(D)$C(O)C_1$-C_4 alkyl,

(D)$C(O)OC_1$-C_4 alkyl,

(D)C(O)heteroaryl,

(D)$N(R^8)_2$,

(D)$NR^8C(O)C_1$-C_4 alkyl,

(D)$NR^8SO_2(C_1$-C_4 alkyl),

(D)OC_1-C_4 alkyl,

(D)$OC(O)C_1$-C_4 alkyl,

(D)heterocyclic,

(D)SC_1-C_4 alkyl, or

(D)$SO_2N(R^8)_2$;

wherein C_1-C_8 alkyl, C_1-C_8 alkoxy, C_3-C_7 cycloalkyl, phenyl, aryl, heterocyclic, and heteroaryl are optionally substituted with one to five substituents independently selected from R^8; and provided that when R is halo or hydroxy it is not substituted on a carbon adjacent to a heteroatom;

each R^8 is independently:

hydrogen,

oxo,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

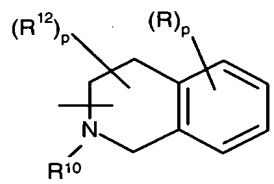
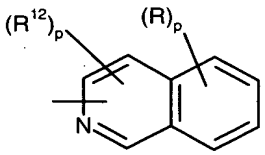
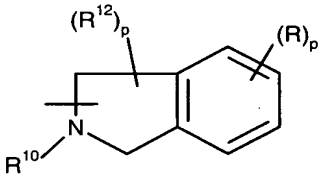
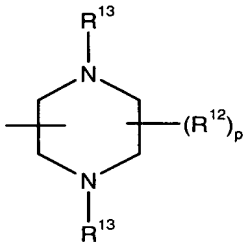
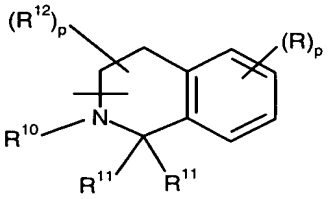
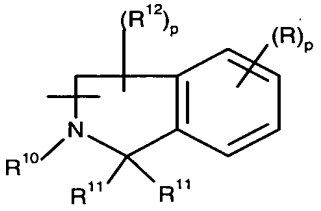
phenyl,

aryl or

heteroaryl,

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to three substituents selected from the group consisting of C_1-C_8 alkyl, halo, and hydroxy; provided that the halo and hydroxy groups are not substituted on a carbon adjacent to a heteroatom;

T is:







;

R^9 is independently:

hydrogen,

(C_1-C_8) alkyl,

C_2-C_8 alkenyl,

$C(O)C_1$-C_8 alkyl,

C_2-C_8 alkynyl,

phenyl,

aryl, or

heteroaryl;

R^{10} is: hydrogen,

$(C_1\text{-}C_8)$ alkyl,

$C_3\text{-}C_8$ alkenyl,

$C(O)C_1\text{-}C_8$ alkyl,

$C_2\text{-}C_8$ alkynyl,

phenyl,

aryl, or

heteroaryl;

R^{11} is independently:

hydrogen, $(C_1\text{-}C_8)$ alkyl, (D)phenyl, or aryl;

R^{12} is independently:

$C_1\text{-}C_8$ alkyl,

phenyl,

aryl,

heteroaryl,

$(CH_2)_nN(R^8)_2$,

$(CH_2)_nNR^8C(O)C_1\text{-}C_4$ alkyl,

$(CH_2)_nNR^8C(O)OC_1\text{-}C_4$ alkyl,

$(CH_2)_n(OCH_2CH_2)_qN(R^8)_2$,

$(CH_2)_n(OCH_2CH_2)_qNR^8C(O)C_1\text{-}C_4$ alkyl,

$(CH_2)_n(OCH_2CH_2)_qNR^8SO_2(C_1\text{-}C_4$ alkyl), or

$(CH_2)_n[O]_q(C_1\text{-}C_8)$alkylheterocyclic; and wherein for R^{12}, n is 2–8 when R^{12} is substituted on a carbon atom adjacent to a heteroatom;

R^{13} is independently:

hydrogen,

$C_1\text{-}C_8$ alkyl,

$(D)C_3\text{-}C_7$ cycloalkyl,

(D)phenyl,

$C(O)C_1$-C_8 alkyl,

SO_2C_1-C_8 alkyl, or

SO_2-phenyl;

D is: a bond or C_1-C_4 alkyl;

g is: 0, 1, or 2;

y is: 1 or 2;

m is: 1-4;

n is: 0-8;

p is: 0-4; and

q is: 0-1.

2. (Original) The compound according to Claim 1 wherein for the Z ring y is 1, or 2

3. (Original) The compound according to Claim 1 wherein the Z ring is saturated.

4. (Original) The compound according to Claim 1 wherein the Z ring is cyclopentyl or cyclohexyl.

5. (Original) The compound according to Claim 3 wherein E is O, S, NR^{1b}, SO_2, SO, or CHR^9.

6. (Presently amended) The compound according to Claim 5 ~~Claim 1~~ wherein E is CH_2.

7. (Original) The compound according to Claim 1 wherein E is CHR^9 and R^9 combines with adjacent R^1 to form a benzene ring.

8. (Original) The compound according to Claim 1 wherein for the Z ring R^1 is hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, C_2-C_4 haloalkyl, (D)C_3-C_7 cycloalkyl, 2-fluorobenzyl, (D)phenyl, $(CH_2)_mC(O)C_1$-C_4 alkyl, $(CH_2)_mN(R^8)_2$, or $(CH_2)_mNR^8C(O)C_1$-C_4 alkyl; D is a bond or CH_2; and p is 1; and m is 1.

9. (Original) The compound according to Claim 1 wherein R is hydrogen, methyl, trifluoromethyl, phenyl or benzyl, wherein phenyl and benzyl groups are optionally substituted with halo or hydroxy and p is 1.

10. (Original) The compound according to Claim 1 wherein R^{1a} is C_1-C_8 alkyl, C_1-C_8 alkenyl, C_2-C_4 haloalkyl, (D)C_3-C_7 cycloalkyl, (D)phenyl, (D)COR^8, (D)$N(R^8)_2$, or (D)NR^8COR^8.

11. (Presently amended) The compound according to Claim 10 ~~Claim 1~~ wherein R^{1a} is isopropyl, isobutyl, cyclohexylmethyl, phenyl, 2-fluorobenzyl or benzyl.

12. (Presently amended) The compound according to Claim 1 ~~Claim 11~~ wherein E is selected from the group consisting of: $-NCH_3$, $-NCH(CH_3)_2$, S, CR^9, $C(R^9)_2$, $-NC(O)CH_3$, $-NC(O)CH(CH_3)_2$, $-NCH_2CH_3$, NSO_2CH_3, and O.

13. (Original) The compound according to Claim 12 wherein E is CR^9 or $C(R^9)_2$, wherein each R^9 is independently selected from hydrogen and C_1-C_4 alkyl, and wherein each R^9 may combine with an adjacent R^1 to form a 5 or 6-member carbocycle.

14. (Original) The compound according to Claim 1 wherein R^2 is hydrogen, C_1-C_8 alkyl, C_1-C_4 haloalkyl, (D)C_3-C_7 cycloalkyl, (D)phenyl, or (D)$C(O)C_1$-C_8 alkyl.

15. (Original) The compound of Claim 1 wherein R^3 is phenyl optionally being para-substituted with chloro, bromo, benzyloxy, methoxy or methyl.

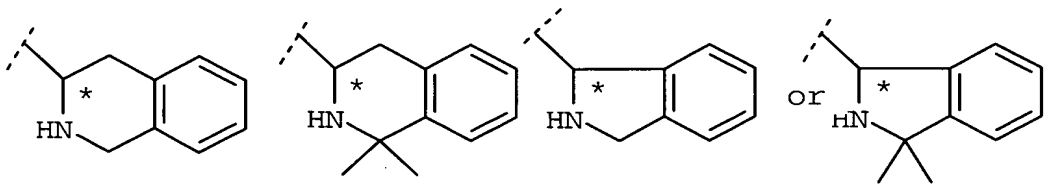
16. (Presently amended) The compound of Claim 15 ~~any one of Claims 1 to 15~~ wherein R^3 is phenyl para-substituted with chloro.

17. (Presently amended) The compound of Claim 1 ~~any one of Claims 1 to 15~~ wherein R^{10} is hydrogen, C_1-C_4 alkyl, or C(O)C1-C4 alkyl.

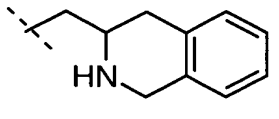
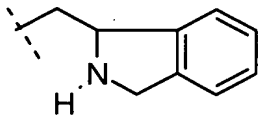
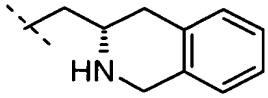
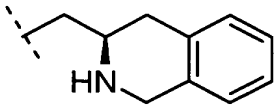
18. (Presently amended) The compound of Claim 17 ~~any one of Claims 1 to 15~~ wherein R^{10} is hydrogen at each occurrence.

19. (Cancelled)

20. (Presently amended) The compound according to Claim 1 ~~Claims 1 to 15~~ wherein "T" is a moiety of the formula:

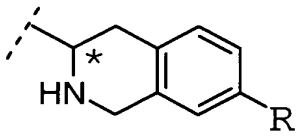


21. (Presently amended) The compound according to Claim 1 ~~any of Claims 1 to 15~~ wherein "T" is a moiety selected from the group consisting of:

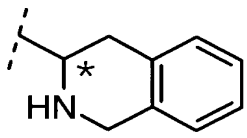
and

22. (Presently amended) The compound of Claim 1 ~~any one of Claims 1 to 15~~ wherein T is a moiety of the formula:

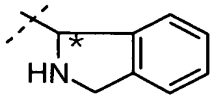


wherein R is as described in Claim 1; and wherein the carbon atom marked * represents a chiral center.

23. (Presently amended) The compound of Claim 1 ~~any one of Claims 1 to 15~~ wherein L and L^1 are each hydrogen; and T is a moiety of the formula:



24. (Presently amended) The compound according to Claim 1 ~~any one of Claims 1 to 15~~ wherein L and L^1 are each hydrogen, and T is a moiety of the formula:



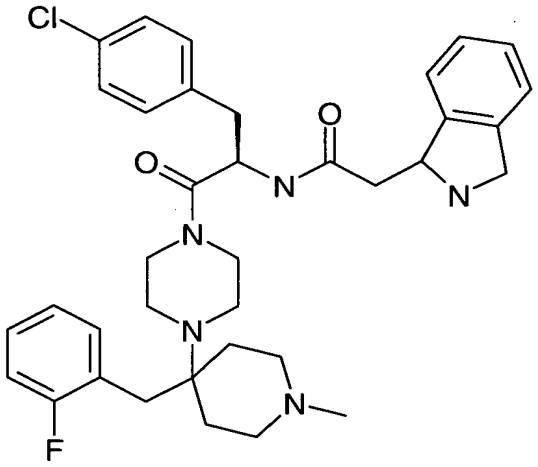
25. (Presently amended) The compound of any one of Claims ~~Claim~~ 22, 23, or 24 wherein the carbon atom marked with * has the R or S configuration.

26. (Cancelled)

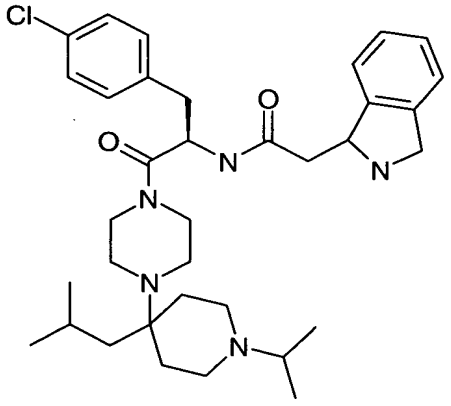
27. (Presently amended) A pharmaceutical composition comprising a compound of Claim 1 ~~any one of Claims 1 25~~ and a pharmaceutical carrier.

28. (Original) The pharmaceutical composition of Claim 27 further comprising a second active ingredient selected from the group consisting of an insulin sensitizer, insulin mimetic, sulfonylurea, alpha-glucosidase inhibitor, HMG-CoA reductase inhibitor, sequestrant cholesterol lowering agent, beta 3 adrenergic receptor agonist, neuropeptide Y antagonist, phosphodiester V inhibitor, and an alpha2 adrenergic receptor antagonist.

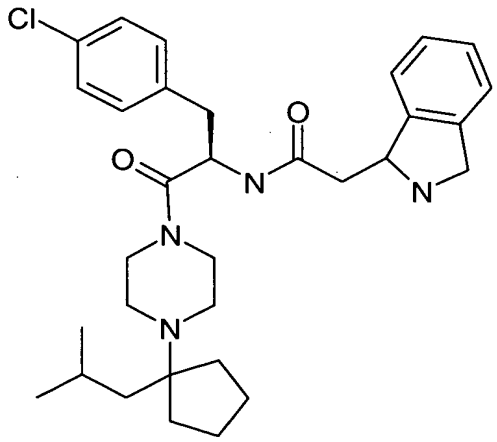
29. (Original) A compound selected from the group consisting of:



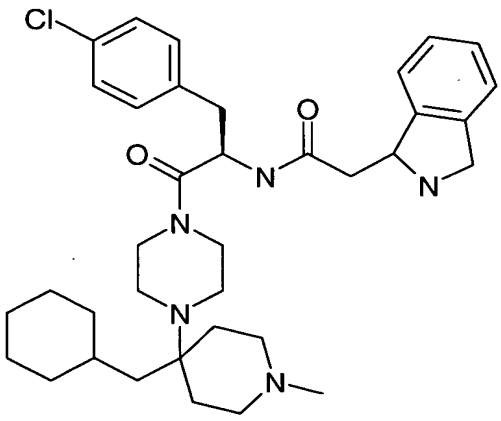
N-(1-(4-Chloro-benzyl)-2-{4-[4-(2-fluoro-benzyl)-1-methyl-piperidin-4-yl]-piperazin-1-yl}-2-oxo-ethyl)-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



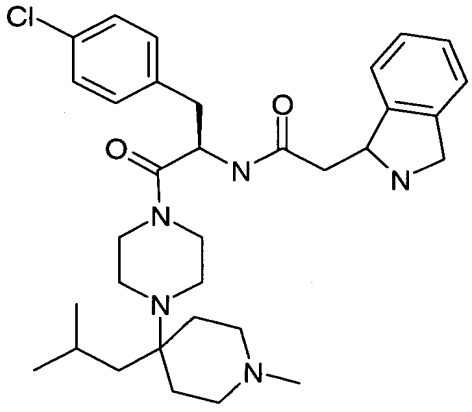
N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1-isopropyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



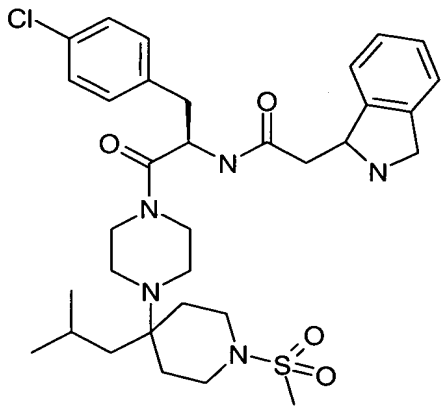
N-{1-(4-Chloro-benzyl)-2-[4-(1-isobutyl-cyclopentyl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



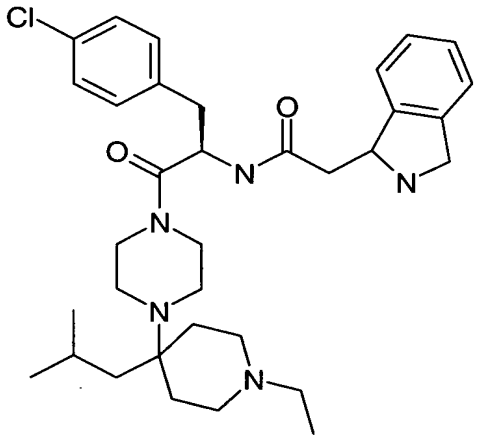
N-{1-(4-Chloro-benzyl)-2-[4-(4-cyclohexylmethyl-1-methyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



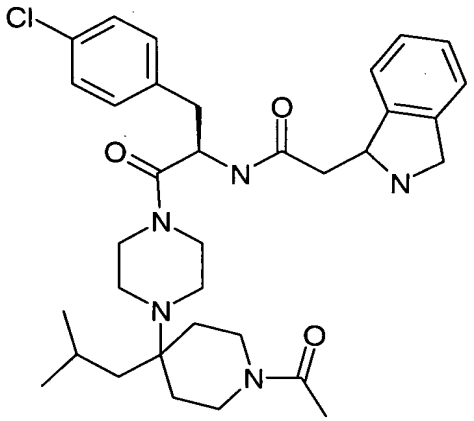
N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1-methyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



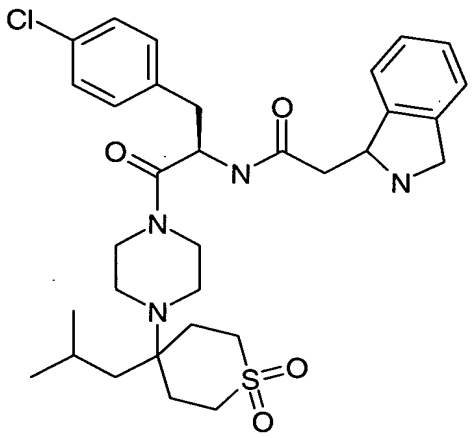
N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1-methanesulfonyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



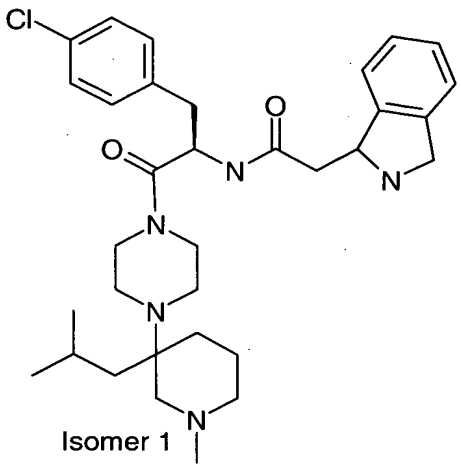
N-{1-(4-Chloro-benzyl)-2-[4-(1-ethyl-4-isobutyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



N-[2-[4-(1-Acetyl-4-isobutyl-piperidin-4-yl)-piperazin-1-yl]-1-(4-chloro-benzyl)-2-oxo-ethyl]-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,

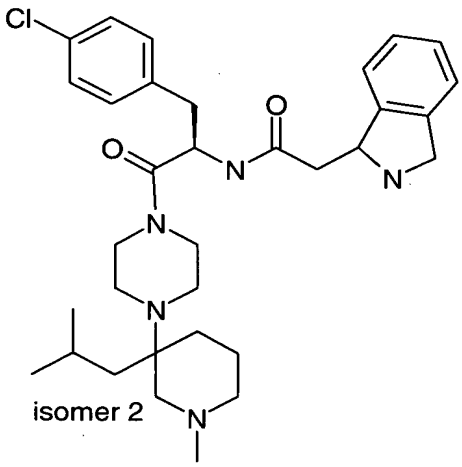


N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1,1-dioxo-hexahydro-1l6-thiopyran-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



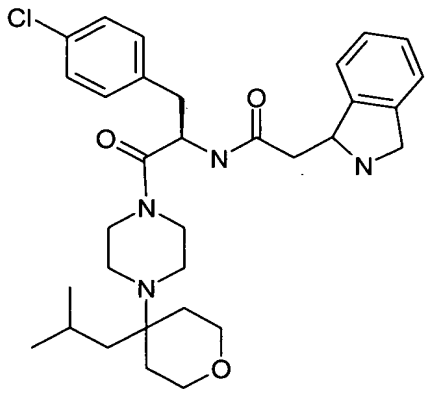
Isomer 1

N-{1-(4-Chloro-benzyl)-2-[4-(3-isobutyl-1-methyl-piperidin-3-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,

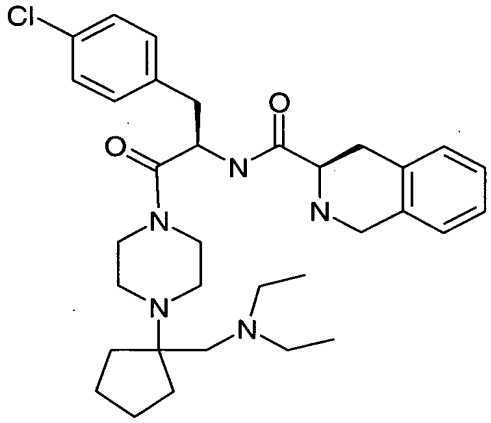


isomer 2

N-{1-(4-Chloro-benzyl)-2-[4-(3-isobutyl-1-methyl-piperidin-3-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,

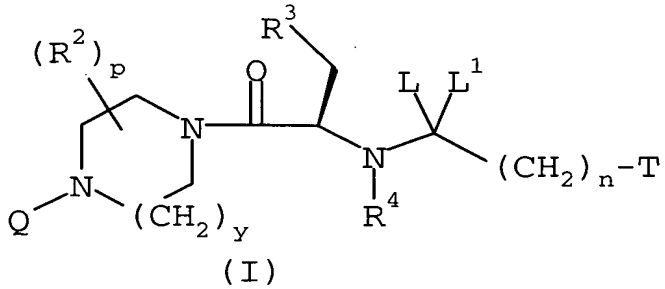


N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-tetrahydro-pyran-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide, and



1,2,3,4-Tetrahydro-isoquinoline-3-carboxylic acid {1-(4-chloro-benzyl)-2-[4-(1-diethylaminomethyl-cyclopentyl)-piperazin-1-yl]-2-oxo-ethyl}-amide, and its pharmaceutically acceptable salt, solvate, prodrug and enantiomer thereof.

30. (Original) A process for preparing a compound of formula I:

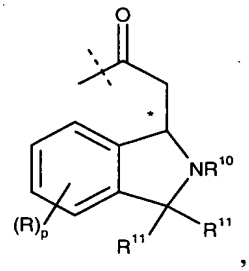


(I)

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

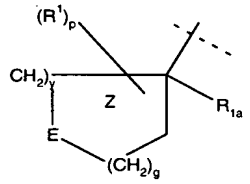
-CLL'-$(CH_2)_n$-T is:



,

R^{10} is a CBz or Boc protecting group, hydrogen, $(C_1\text{-}C_8)$ alkyl, $C_3\text{-}C_8$ alkenyl, $C(O)C_1\text{-}C_8$ alkyl, $C_2\text{-}C_8$ alkynyl, phenyl, aryl, or heteroaryl;

Q is represent the moiety:



,

L and L^1 are both hydrogen or combine together to form an oxo group;

E is: O, S, NR^{1b}, SO, SO_2, CR^9, or $C(R^9)_2$, provided that when E is CR^9, or $C(R^9)_2$, R^9 may combine with an adjacent R^1 to form a 5, 6, or 7-member saturated or unsaturated carbocycle;

wherein the Z ring has 0, or 1 double bond;

R^1 is selected from the group consisting of:

hydrogen,

$C_1\text{-}C_8$ alkyl,

$C_2\text{-}C_8$ alkenyl,

$C_2\text{-}C_4$ haloalkyl

(D)$C_3\text{-}C_7$ cycloalkyl,

(D)phenyl,

aryl,

$C(O)OC_1\text{-}C_8$ alkyl,

wherein phenyl, aryl, alkenyl, and cycloalkyl groups are optionally substituted with hydroxy, halo, C_1-C_8 alkyl, C_1-C_4 alkoxy, C_2-C_4 haloalkyl, and (D)C_3-C_7 cycloalkyl provided that the halo, hydroxy are not substituted on a carbon atom adjacent to a heteroatom;

R_{1a} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

(D)aryl,

(D)heteroaryl;

(D)C(O)C_1-C_4 alkyl,

(D)C(O)OC_1-C_4 alkyl,

$(CH_2)_mN(R^8)_2$,

$(CH_2)_mNR^8C(O)C_1$-C_4 alkyl,

$(CH_2)_mNR^8SO_2(C_1$-C_4 alkyl),

$(CH_2)_mOR^8$,

$(CH_2)_mSC_1$-C_4 alkyl,

$(CH_2)_mSO(C_1$-C_4 alkyl),

$(CH_2)_mSO_2(C_1$-C_4 alkyl), or

$(CH_2)_mSO_2\ N(R^8)_2$;

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to five substituents independently selected from the group consisting of perfluoroC_1-C_4 alkoxy, halo, hydroxy, C_1-C_8 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl; provided that halo and hydroxy groups are not substituted on a carbon atom adjacent to a heteroatom;

R^{1b} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

$SO_2(C_1\text{-}C_8$ alkyl),

(D)$C(O)C_1\text{-}C_4$ alkyl,

(D)$C(O)OC_1\text{-}C_4$ alkyl,

(D)$CON(R^8)2$, or

SO_2(D)phenyl, wherein the phenyl group is optionally substituted with one to five substituents selected from halo, and $C_1\text{-}C_8$ alkyl;

R^2 is: hydrogen,

$C_1\text{-}C_8$ alkyl,

$CONHC_1\text{-}C_4$ alkyl,

(D)phenyl,

oxo, or

(D)$C_3\text{-}C_7$ cycloalkyl, provided that when R^2 is oxo, R^2 is on one of the ring carbon atoms adjacent to the nitrogen atom bearing the Z ring;

R^3 is: phenyl, aryl or thienyl;

wherein phenyl, aryl and thienyl are optionally substituted with one to three substituents independently selected from the group consisting of:

cyano, perfluoro$C_1\text{-}C_4$ alkoxy, halo, $C_1\text{-}C_8$ alkyl, (D)$C_3\text{-}C_7$ cycloalkyl, $C_1\text{-}C_4$ alkoxy, $C_1\text{-}C_4$ haloalkyl;

R^4 is: hydrogen,

$C_1\text{-}C_8$ alkyl,

$CH_2(CH_2)_mC_1\text{-}C_4$ alkoxy,

$C(O)C_1\text{-}C_4$ alkyl, or

$C(O)OC_1\text{-}C_4$ alkyl;

R is: hydroxy,

halo,

$C_1\text{-}C_8$ alkyl,

C_2-C_8 alkenyl,

C_1-C_8 alkoxy,

C_1-C_4 haloalkyl,

(D)C_3-C_7 cycloalkyl,

(D)aryl,

(D)heteroaryl;

(D)C(O)C_1-C_4 alkyl,

(D)C(O)OC_1-C_4 alkyl,

(D)C(O)heteroaryl,

(D)N(R^8)$_2$,

(D)NR^8C(O)C_1-C_4 alkyl,

(D)NR^8SO_2(C_1-C_4 alkyl),

(D)OC_1-C_4 alkyl,

(D)OC(O)C_1-C_4 alkyl,

(D)heterocyclic,

(D)SC_1-C_4 alkyl, or

(D)SO_2N(R^8)$_2$;

wherein C_1-C_8 alkyl, C_1-C_8 alkoxy, C_3-C_7 cycloalkyl, phenyl, aryl, heterocyclic, and heteroaryl are optionally substituted with one to five substituents independently selected from R^8; and provided that when R is halo or hydroxy it is not substituted on a carbon adjacent to a heteroatom;

each R^8 is independently:

hydrogen,

oxo,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

phenyl,

aryl or

heteroaryl,

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to three substituents selected from the group consisting of C_1-C_8 alkyl, halo, and hydroxy; provided that the halo and hydroxy groups are not substituted on a carbon adjacent to a heteroatom;

R^9 is independently hydrogen, (C_1-C_8) alkyl, C_2-C_8 alkenyl, $C(O)C_1$-C_8 alkyl, C_2-C_8 alkynyl, phenyl, aryl, or heteroaryl;

R^{11} is independently:

hydrogen, (C_1-C_8) alkyl, (D)phenyl or aryl;

D is: a bond or C_1-C_4 alkyl;

g is: 0, 1, or 2;

y is: 1 or 2;

m is: 1-4;

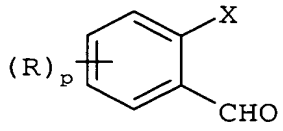
n is: 0-8;

p is: 0-4; and

q is: 0-1;

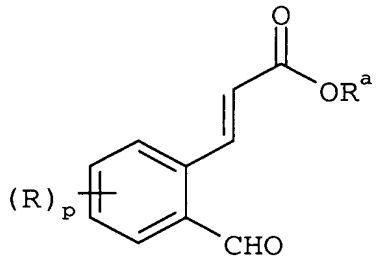
comprising the steps of:

a) reacting a compound having a structural formula 1:



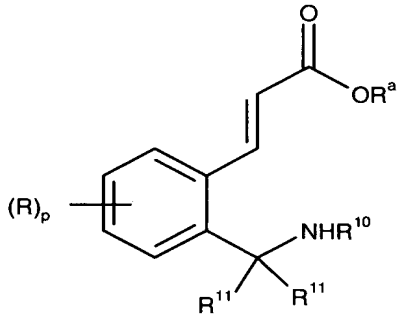
(1)

with $CH_2CH=C(O)OR^a$ wherein R^a is hydrogen or C_1-C_8 alkyl and X is halo, in the presence of a catalyst and a base in a suitable organic solvent to give the compound of formula 2:



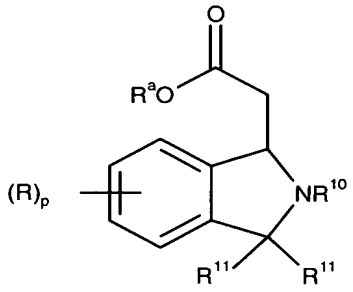
(2);

b) reductively aminating the compound of formula 2 in the presence of amine in an acidic condition to give a compound of formula 3:



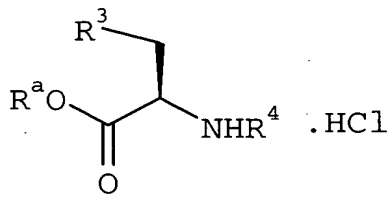
(3);

c) cyclizing the compound of formula 3 by Michael addition to give a compound of formula 4 or stereoisomers thereof:



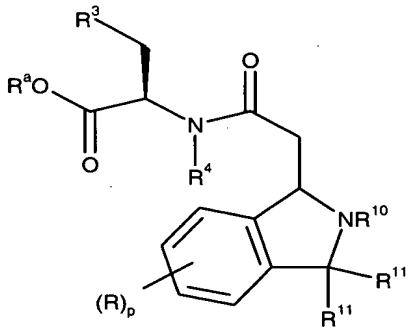
(4);

d) coupling the compound of formula 4 or stereoisomers thereof wherein R^a is H, with a compound of formula 5:



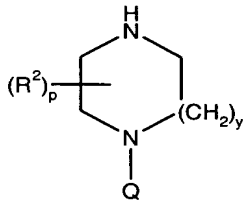
(5);

wherein R^a is C_1-C_8 alkyl, to give a compound of formula 6:



(6); and

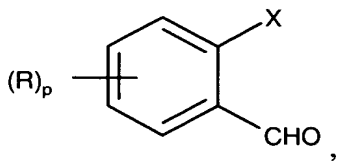
e) coupling the compound of formula 6 wherein R^a is H, with a compound having a structural formula:



,

to afford the compound of formula 1.

31. (Original) The process of Claim 30, wherein:



,

in Step a) is 2-boromobenzaldehyde.

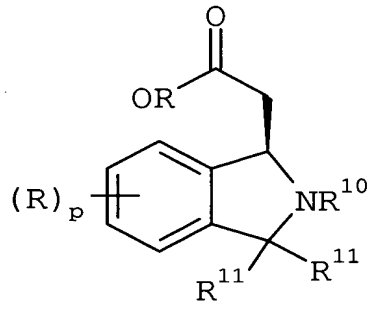
32. (Presently amended) The process of Claim 30 ~~Claim 31~~, wherein $CH_2CH=C(O)OR^a$ in Step (a) is methylacrylate.

33. (Presently amended) The process of Claim 30 ~~Claim 32~~, wherein the catalyst in Step (a) is selected from the group consisting of: $Pd(Ph_3P)_2Cl_2$, $Pd(Ph_3P)_4Cl_2$, $Pd(Ph_3P)_4$, $Pd(Ph_3P)_2Cl_2/CuI$, $Pd(OAc)_2/Ph_3P\text{-}Bu_4NBr$, $Pd(Ph_3P)_4Cl_2/H_2$ and $Pd(OAc)_2/P(O\text{-}tol)_3$; and wherein the base in Step (a) is $N(R)_3$ where R is hydrogen or C_1-C_8 alkyl.

34. (Presently amended) The process of Claim 30 ~~Claim 33~~, wherein the amine in Step (b) is selected from the group consisting of: benzylamine, alpha-methylbenzylamine and $BocNH_2$.

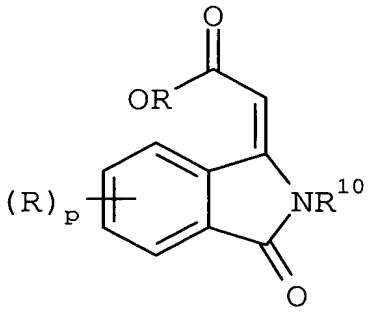
35. (Original) The process of Claim 34, wherein Step (b) further comprises the step of reducing an intermediate imine compound in the presence of reducing agent selected from the group consisting of: $NaCNBH_3$, $Na(OAc)_3BH$, $NaBH_4/H+$ and a combination of Et_3SiH and TFA in CH_3CN or CH_2Cl_2.

36. (Presently amended) The process of Claim 30 ~~31~~, wherein the stereoisomer of compound of formula (4) ~~(7)~~ in Step (c) is a compound of formula 7a:



(7a).

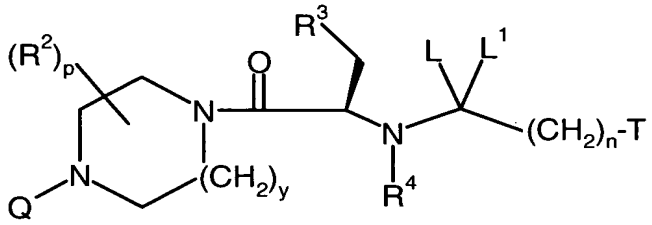
37. (Original) The process of Claim 36, wherein the compound of formula 7a is prepared by asymmetric hydrogenation of a compound having structural formula,



38. (Presently amended) The process of Claim 30 ~~31~~, wherein the Michael addition in Step (c) is carried out under basic workup condition.

39. (Presently amended) The process of Claim 30 ~~31~~, wherein the Step (e) further comprises deprotecting or protecting of the compound of formula (4) at NR^{10}.

40. (Original) A process for preparing a compound of formula I:

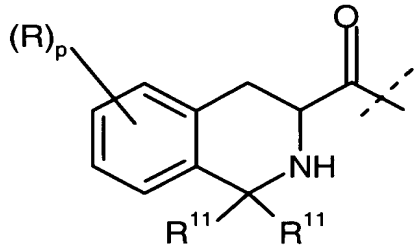


(I)

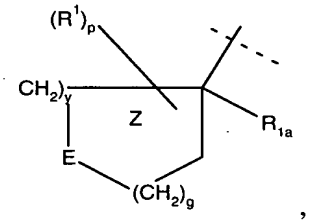
or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

$-LL'(CH_2)_n$-T is represented by the group:



and Q represents the moiety:



,

E is: O, S, NR^{1b}, SO, SO_2, CR^9, or $C(R^9)_2$, provided that when E is CR^9, or $C(R^9)_2$, R^9 may combine with an adjacent R^1 to form a 5, 6, or 7-member saturated or unsaturated carbocycle;

wherein the Z ring has 0, or 1 double bond;

R^1 is selected from the group consisting of:

hydrogen,

C_1-C_8 alkyl,

C_2-C_8 alkenyl,

C_2-C_4 haloalkyl

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

aryl,

$C(O)OC_1$-C_8 alkyl,

wherein phenyl, aryl, alkenyl, and cycloalkyl groups are optionally substituted with hydroxy, halo, C_1-C_8 alkyl, C_1-C_4 alkoxy, C_2-C_4 haloalkyl, and (D)C_3-C_7 cycloalkyl provided that the halo, hydroxy are not substituted on a carbon atom adjacent to a heteroatom;

R_{1a} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

(D)aryl,

(D)heteroaryl;

(D)$C(O)C_1$-C_4 alkyl,

(D)$C(O)OC_1$-C_4 alkyl,

$(CH_2)_mN(R^8)_2$,

$(CH_2)_mNR^8C(O)C_1$-C_4 alkyl,

$(CH_2)_mNR^8SO_2(C_1$-C_4 alkyl),

$(CH_2)_mOR^8$,

$(CH_2)_mSC_1$-C_4 alkyl,

$(CH_2)_mSO(C_1$-C_4 alkyl),

$(CH_2)_mSO_2(C_1$-C_4 alkyl), or

$(CH_2)_mSO_2\ N(R^8)_2$;

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to five substituents independently selected from the group consisting of perfluoroC_1-C_4 alkoxy, halo, hydroxy, C_1-C_8 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl; provided that halo and hydroxy groups are not substituted on a carbon atom adjacent to a heteroatom;

R^{1b} is: hydrogen,
C_1-C_8 alkyl,
(D)C_3-C_7 cycloalkyl,
SO_2(C_1-C_8 alkyl),
(D)C(O)C_1-C_4 alkyl,
(D)C(O)OC_1-C_4 alkyl,
(D)CON(R^8)2, or
SO_2(D)phenyl, wherein the phenyl group is optionally substituted with one to five substituent selected from halo, and C_1-C_8 alkyl;

R^2 is: hydrogen,
C_1-C_8 alkyl,
CONHC_1-C_4 alkyl,
(D)phenyl,
oxo, or
(D)C_3-C_7 cycloalkyl, provided that when R^2 is oxo, R^2 is on one of the ring carbon atoms adjacent to the nitrogen atom bearing the Z ring;

R^3 is: phenyl, aryl or thienyl;
wherein phenyl, aryl and thienyl are optionally substituted with one to three substituents independently selected from the group consisting of:
cyano, perfluoroC_1-C_4 alkoxy, halo, C_1-C_8 alkyl, (D)C_3-C_7 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl;

R^4 is: hydrogen,

C_1-C_8 alkyl,

$CH_2(CH_2)_mC_1$-C_4 alkoxy,

$C(O)C_1$-C_4 alkyl or

$C(O)OC_1$-C_4 alkyl;

R is: hydroxy,

halo,

C_1-C_8 alkyl,

C_2-C_8 alkenyl,

C_1-C_8 alkoxy,

C_1-C_4 haloalkyl,

(D)C_3-C_7 cycloalkyl,

(D)aryl,

(D)heteroaryl;

(D)$C(O)C_1$-C_4 alkyl,

(D)$C(O)OC_1$-C_4 alkyl,

(D)C(O)heteroaryl,

(D)$N(R^8)_2$,

(D)$NR^8C(O)C_1$-C_4 alkyl,

(D)$NR^8SO_2(C_1$-C_4 alkyl),

(D)OC_1-C_4 alkyl,

(D)$OC(O)C_1$-C_4 alkyl,

(D)heterocyclic,

(D)SC_1-C_4 alkyl, or

(D)$SO_2N(R^8)_2$;

wherein C_1-C_8 alkyl, C_1-C_8 alkoxy, C_3-C_7 cycloalkyl, phenyl, aryl, heterocyclic, and heteroaryl are optionally substituted with one to five substituents independently selected from R^8; and provided that when R is halo or hydroxy it is not substituted on a carbon adjacent to a heteroatom;

each R^8 is independently:

hydrogen,

oxo,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

phenyl,

aryl or

heteroaryl,

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to three substituents selected from the group consisting of C_1-C_8 alkyl, halo, and hydroxy; provided that the halo and hydroxy groups are not substituted on a carbon adjacent to a heteroatom;

R^9 is independently:

hydrogen,

(C_1-C_8) alkyl,

C_2-C_8 alkenyl,

C(O)C_1-C_8 alkyl,

C_2-C_8 alkynyl,

phenyl,

aryl, or

heteroaryl;

R^{10} is: hydrogen,

(C_1-C_8) alkyl,

C_3-C_8 alkenyl,

$C(O)C_1$-C_8 alkyl,

C_2-C_8 alkynyl,

phenyl,

aryl, or

heteroaryl;

R^{11} is independently:

hydrogen, (C_1-C_8) alkyl, or (D)phenyl, or aryl;

D is: a bond or C_1-C_4 alkyl;

g is: 0, 1, or 2;

y is: 1 or 2;

m is: 1-4;

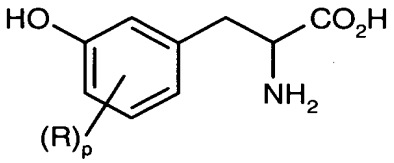
n is: 0-8;

p is: 0-4; and

q is: 0-1;

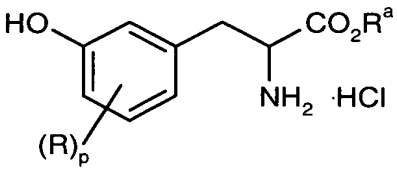
comprising the steps of:

a) esterifying a compound of formula 1 with an alcohol R^aOH



1;

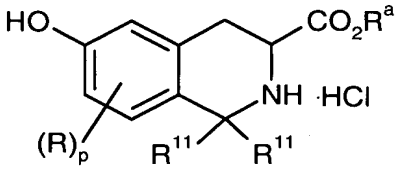
to form a compound of formula 2:



2;

wherein R^a is a group selected from C_1-C_4 alkyl, and (D) phenyl;

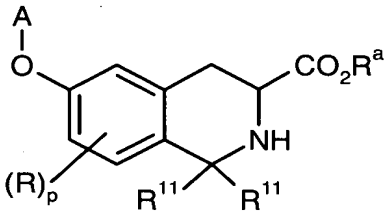
b) reacting a compound of formula 2 with $R^{11}COR^{11}$ to form a compound of formula:



3;

wherein R^{11} is independently hydrogen, C_1-C_4 alkyl;

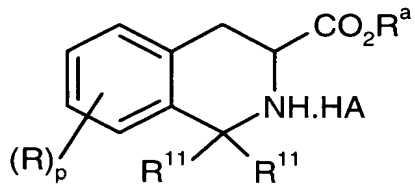
c) reacting a compound of formula 3 with an activating group to form a compound of formula 4:



4 ;

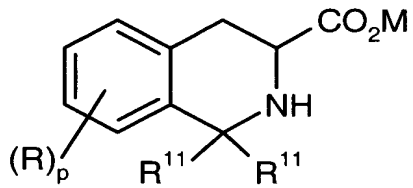
wherein A is an activating group;

d) deoxygenating the compound of formula 4 by hydrogenation to afford a compound of formula 5:



5;

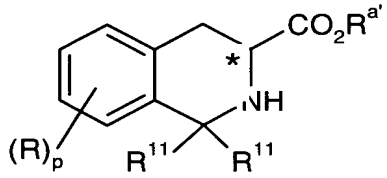
e) optionally reacting the compound of formula 5 wherein HA is an acidic, with an inorganic base to form a compound of formula 6:



6;

wherein M is a univalent cation;

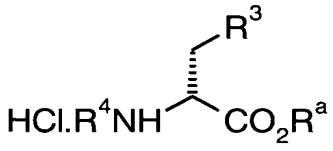
f) resolving the compound of formula 5 or the compound of formula 6 wherein M is hydrogen to afford a chiral compound of formula 7:



7;

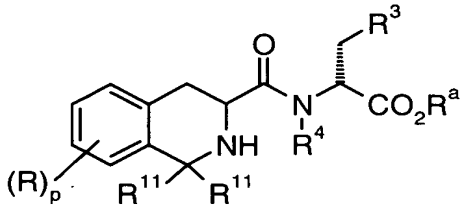
wherein Ra' is H or R^a;

g) coupling the compound of formula 7 with a compound of formula 8:



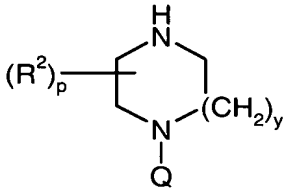
8;

to afford a compound of formula 9:



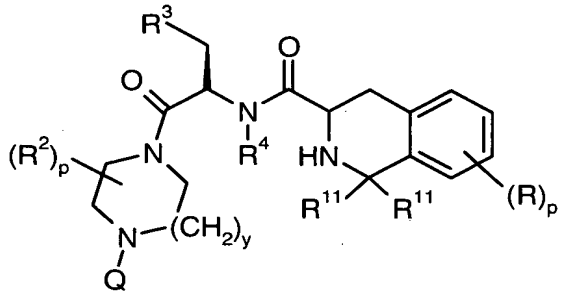
9;

h) coupling the compound of formula 9 with a compound of formula 10:



10;

to afford a compound of formula I:

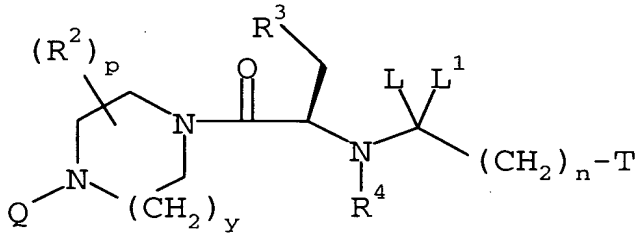


I.

41. (Original) The process according to Claim 40 wherein the esterification is performed via an acylhalide intermediate formed by reaction of compound (1) with thionyl chloride, or oxalylchloride.

42. (Presently amended) The process according to Claim 40 ~~Claim 41~~ wherein the activating agent is trifluoromethanesulfonic anhydride to form the triflate.

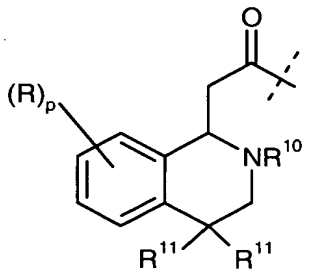
43. (Original) A process for preparing a compound of formula I:



(I)

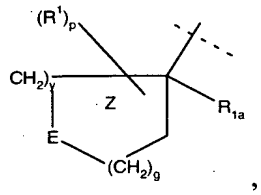
or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein $-LL'(CH_2)_n-T$ is represented by the group:



R^{10} is a CBz or Boc protecting group, hydrogen, (C_1-C_8) alkyl, C_3-C_8 alkenyl, $C(O)C_1-C_8$ alkyl, C_2-C_8 alkynyl, phenyl, aryl, or heteroaryl;

Q represents the moiety:



E is: O, S, NR^{1b}, SO, SO_2, CR^9, or $C(R^9)_2$, provided that when E is CR^9, or $C(R^9)_2$, R^9 may combine with an adjacent R^1 to form a 5, 6, or 7-member saturated or unsaturated carbocycle;

wherein the Z ring has 0, or 1 double bond;

R^1 is selected from the group consisting of:

hydrogen,

C_1-C_8 alkyl,

C_2-C_8 alkenyl,

C_2-C_4 haloalkyl

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

aryl,

$C(O)OC_1$-C_8 alkyl,

wherein phenyl, aryl alkenyl,and cycloalkyl groups are optionally substituted with hydroxy, halo, C_1-C_8 alkyl, C_1-C_4 alkoxy, C_2-C_4 haloalkyl, and (D)C_3-C_7 cycloalkyl provided that the halo, hydroxy are not substituted on a carbon atom adjacent to a heteroatom;

R_{1a} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

(D)aryl,

(D)heteroaryl;

(D)$C(O)C_1$-C_4 alkyl,

(D)$C(O)OC_1$-C_4 alkyl,

$(CH_2)_mN(R^8)_2$,

$(CH_2)_mNR^8C(O)C_1$-C_4 alkyl,

$(CH_2)_mNR^8SO_2(C_1$-C_4 alkyl),

$(CH_2)_mOR^8$,

$(CH_2)_mSC_1$-C_4 alkyl,

$(CH_2)_mSO(C_1$-C_4 alkyl),

$(CH_2)_mSO_2(C_1$-C_4 alkyl), or

$(CH_2)_mSO_2\ N(R^8)_2$;

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to five substituents independently selected from the group consisting of perfluoroC_1-C_4 alkoxy, halo, hydroxy, C_1-C_8 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl; provided that halo and hydroxy groups are not substituted on a carbon atom adjacent to a heteroatom;

R^{1b} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

$SO_2(C_1$-C_8 alkyl),

(D)$C(O)C_1$-C_4 alkyl,

(D)$C(O)OC_1$-C_4 alkyl,

(D)$CON(R^8)2$, or

SO_2(D)phenyl, wherein the phenyl group is optionally substituted with one to 1 to 5 substituent selected from halo, and C_1-C_8 alkyl;

R^2 is: hydrogen,

C_1-C_8 alkyl,

$CONHC_1$-C_4 alkyl,

(D)phenyl, oxo, or

(D)C_3-C_7 cycloalkyl, provided that when R^2 is oxo, R^2 is on one of the ring carbon atoms adjacent to the nitrogen atom bearing the Z ring;

R^3 is: phenyl, aryl or thienyl;
wherein phenyl, aryl and thienyl are optionally substituted with one to three substituents independently selected from the group consisting of:
cyano, perfluoroC_1-C_4 alkoxy, halo, C_1-C_8 alkyl, (D)C_3-C_7 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl;

R^4 is: hydrogen,
C_1-C_8 alkyl,
$CH_2(CH_2)_mC_1$-C_4 alkoxy,
$C(O)C_1$-C_4 alkyl, or
$C(O)OC_1$-C_4 alkyl;

R is: hydroxy,
halo,
C_1-C_8 alkyl,
C_2-C_8 alkenyl,
C_1-C_8 alkoxy,
C_1-C_4 haloalkyl,
(D)C_3-C_7 cycloalkyl,
(D)aryl,
(D)heteroaryl;
(D)$C(O)C_1$-C_4 alkyl,
(D)$C(O)OC_1$-C_4 alkyl,
(D)C(O)heteroaryl,
(D)$N(R^8)_2$,
(D)$NR^8C(O)C_1$-C_4 alkyl,

(D)NR^8SO_2(C_1-C_4 alkyl),

(D)OC_1-C_4 alkyl,

(D)$OC(O)C_1$-C_4 alkyl,

(D)heterocyclic,

(D)SC_1-C_4 alkyl, or

(D)$SO_2N(R^8)_2$;

wherein C_1-C_8 alkyl, C_1-C_8 alkoxy, C_3-C_7 cycloalkyl, phenyl, aryl, heterocyclic, and heteroaryl are optionally substituted with one to five substituents independently selected from R^8; and provided that when R is halo or hydroxy it is not substituted on a carbon adjacent to a heteroatom;

each R^8 is independently:

hydrogen,

oxo,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

phenyl,

aryl or

heteroaryl,

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, aryl and heteroaryl are optionally substituted with one to three substituents selected from the group consisting of C_1-C_8 alkyl, halo, and hydroxy; provided that the halo and hydroxy groups are not substituted on a carbon adjacent to a heteroatom;

R^9 is independently:

hydrogen,

(C_1-C_8) alkyl,

C_2-C_8 alkenyl,

$C(O)C_1$-C_8 alkyl,

C_2-C_8 alkynyl,

phenyl,

aryl, or

heteroaryl;

R^{11} is independently:

hydrogen, (C_1-C_8) alkyl, or (D)phenyl, aryl;

D is: a bond or C_1-C_4 alkyl;

g is: 0, 1, or 2;

y is: 1 or 2;

m is: 1-4;

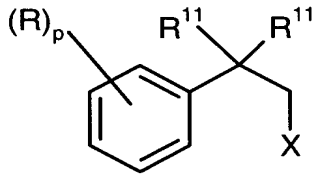
n is: 0-8;

p is: 0-4; and

q is: 0-1;

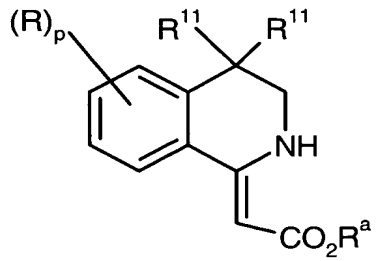
comprising the steps of:

a) reacting a compound formula 1:



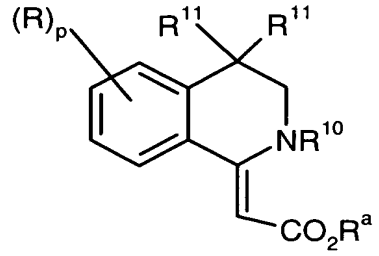
1;

wherein X is halo and R^{11} is independently, hydrogen or C1-C4 alkyl, with $CNCH_2CO_2R^a$ wherein R^a is C_1-C_8 alkyl, or benzyl to afford a compound of formula 2:



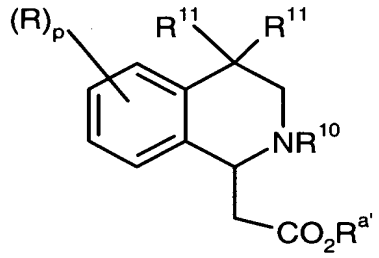
2;

b) protecting the compound of formula 2 to form the compound of formula 3:



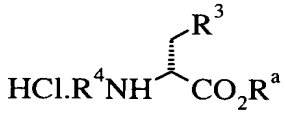
3;

c) hydrogenating the compound of formula 3 to afford a compound of formula 4:



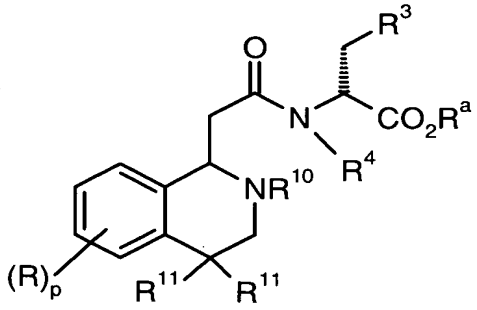
4;

d) coupling the compound of formula 4 wherein $R^{a'}$ is hydrogen with a compound of formula 5:



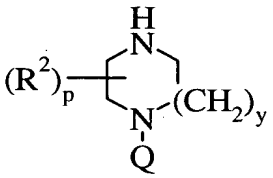
5;

to afford a compound of formula 6:



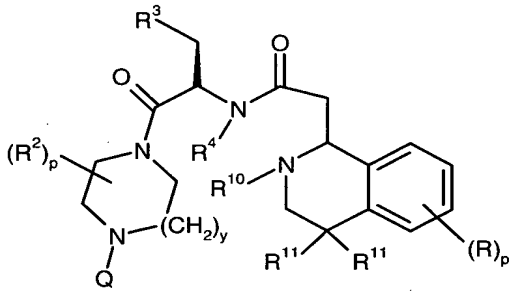
6;

e) coupling the compound of formula 6 with a compound of formula 7:



7;

to afford a compound of formula I:



I.

44. (Original) A method of preventing or treating obesity in a mammal comprising the administration of a therapeutically effective amount of the compound of formula I as recited in Claim 1.

45. (Original) A method of preventing or treating diabetes mellitus in a mammal comprising the administration of a therapeutically effective amount of the compound of formula I as recited in Claim 1.

46. (Original) A method of preventing or treating male or female sexual dysfunction in a mammal comprising the administration of a therapeutically effective amount of the compound of formula I as recited in Claim 1.

47. (Original) The method of 46, wherein the male or female sexual dysfunction is erectile dysfunction.